Echocardiographic Evaluation of Pulmonary Embolism: A Review

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Pulmonary embolism (PE) is the third most common cause of cardiovascular death in the United States. Appropriate risk stratification is an important component of the initial evaluation for acute management of these patients. Echocardiography plays a crucial role in the risk stratification of patients with PE. In this literature review, we describe the current strategies in risk stratification of patients with PE using echocardiography and the role of echocardiography in the diagnosis of PE. (J Am Soc Echocardiogr 2023;■:■-■.)

Keywords: Echocardiography, Pulmonary embolism, Hemodynamics, Right ventricle

INTRODUCTION

Venous thromboembolism (VTE) represents a major cause of morbidity and mortality, with an incidence of approximately 900,000 cases annually in the United States.[1] After myocardial infarction and stroke, pulmonary embolism (PE) forms the third most common cause of cardiovascular death.[2] Pulmonary embolism has an estimated incidence of 117 cases per 100,000 people in the United States, although the incidence rate is likely underestimated given the high likelihood of silent PEs in patients with deep vein thrombosis (DVT).[3,4]

Even though there are approximately 60,000 to 300,000 deaths attributed to PE, most of which occur in inpatients, historical trends have indicated that PE-related mortality has been decreasing.[5,6] Pulmonary embolism is an independent predictor of death for up to 3 months after the event, and the risk is 18-fold higher when compared to patients with only DVT.[7]

The diagnosis and management of PE is based on a combined picture of pretest probability, D-dimer levels, electrocardiogram, computed tomography (CT) pulmonary angiography (CT-PA), and transthoracic echocardiography (TTE). Risk stratification for this disease process relies significantly upon accurate assessment of right ventricular (RV) function, which is a powerful predictor of cardiopulmonary morbidity and mortality.[8] In this literature review, we describe the current strategies for risk stratification and echocardiographic evaluation of PE. Echocardiographic assessment of PE includes the following components: RV size, McConnell's sign, the 60/60 sign, RV systolic function including tricuspid annular planar systolic excursion (TAPSE), RV fractional area change (FAC), TAPSE/pulmonary artery systolic pressure (PASP) ratio, left ventricular outflow tract (LVOT) velocity-time integral (VTI), RV outflow tract (RVOT) VTI, PASP/left ventricular stroke volume (LVSV), and visualization of thrombus in transit.

DIAGNOSTIC EVALUATION OF PE

Pretest Probability and Imaging

Computed tomography pulmonary angiography is the mainstay for the definitive diagnosis of PE. The decision to pursue CT-PA is based on pretest probability. The Wells score calculates a pretest probability for PE, and a score of greater than 4 is a recommendation for such imaging.[9] The Wells score consists of 7 criteria, one of which is "pulmonary embolism is the most likely diagnosis," with a weight of 3 points. As the Wells score has been criticized for being subjective due to this criterion, there are other less subjective scores that define pretest probability, such as PE rule-out criteria (PERC) and the Geneva score, which can also be used. The PERC uses clinical criteria such as age, heart rate, oxygen saturation, leg swelling, hemoptysis, and risk factors such as recent surgery/trauma, prior history of VTE, or hormone use.[10] This can be used in patients that are clinically low risk to rule out a PE. The Geneva score is another score that uses a combination of patient characteristics, VTE risk factors, signs, symptoms, chest x-ray findings, and blood gases to evaluate a patient's pretest probability.[11]

Echocardiography can be useful in the management of PE, mainly as a prognostic tool and less often as a diagnostic tool. It can be used to assess for RV dysfunction if PE is suspected and CT-PA is not immediately available or is clinically contraindicated. We describe the various ways echocardiographic findings can help in PE management below.

RISK STRATIFICATION

Based on PE severity and the risk of in-hospital and 30-day mortality, the European Society of Cardiology (ESC) classifies PE into 4 categories–low risk, intermediate-low, intermediate-high, and high

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Abbreviations

CT = Computed tomography

CT-PA = Computed tomography pulmonary angiography

DVT = Deep vein thrombosis

EF = Ejection fraction

ESC = European Society of Cardiology

ESN = Early systolic notching

FAC = Fractional area change

IVC = Inferior vena cava

LV = Left ventricle

LVOT = Left ventricular outflow tract

LVSV = Left ventricular stroke volume

OR = Odds ratio

PASP = Pulmonary artery systolic pressure

PE = Pulmonary embolism

PERC = Pulmonary embolism rule-out criteria

PERT = Pulmonary embolism response team

PVR = Pulmonary vascular resistance

PW = Pulsed wave

RAP = Right atrial pressure

RV = Right ventricular, ventricle

RVOT = Right ventricular outflow tract

TAPSE = Tricuspid annular planar systolic excursion

TTE = Transthoracic echocardiography

VTE = Venous thromboembolism

VTI = Velocity-time integral

risk.[12] The American Heart Association has classified the severity of PE into low risk, submassive, and massive PE, the difference being that both of the intermediate-risk groups are grouped together to be called submassive PE.[13]

High-risk PE is defined as patients with hemodynamic instability (systolic blood pressures <90 mm Hg or use of vasopressors to maintain systolic blood pressure of ≥90 mm Hg), a confirmed PE diagnosis by CT-PA, and/or signs of RV dysfunction on TTE. The findings of obstructive shock along with confirmation of PE and RV dysfunction are enough to classify a patient into the high-risk category. Hemodynamically stable patients with imaging (TTE and/or CT-PA) and laboratory evidence (elevated troponins) of RV dysfunction are labeled as intermediate-high risk, whereas hemodynamically stable patients with imaging or laboratory evidence of RV dysfunction are labeled as intermediate-low risk. Lastly, hemodynamically stable patients without any evidence of RV dysfunction are considered low risk. It is not necessary to check troponins to risk stratify these low-risk patients.

The previously mentioned ESC guidelines, hemodynamics, CT-PA, echocardiography, and cardiac biomarker testing are all considered mainstays of diagnosis and risk stratification.

Echocardiography in Acute PE

Certain findings when seen on TTE can help support the diagnosis of PE, while other findings can aid in further risk stratification of PE. Right ventricular pressure overload and dysfunction caused by acute pulmonary emboli can be detected by echocardiogram. There are multiple echocardiographic parameters that can be found in the presence of acute PE, none of which are completely reliable to diagnose PE. The role of echocardiography in the management of PE is to primarily risk stratify patients and in some situations can help confirm the diagnosis of PE in patients with high pretest probability and the absence of other comorbid conditions. This is because certain signs of RV dysfunction can also be present in the absence of PE and because of other cardiopulmonary diseases, thereby emphasizing the importance of pretest probability in these patients. These echocardiographic findings have been summarized in Figure 1. With a sensitivity of approximately 50% and a negative predictive value of 40% to 50%, a negative echocardiogram does not completely rule out a PE.[12,14] Hence, it does not perform well as a screening tool.

Echocardiography can be primarily used for prognostic purposes in both hemodynamically stable and unstable PE patients. In hemodynamically stable patients, an echocardiogram can be used to rule out other causes of shortness of breath. Also, in a hemodynamically stable PE patient with elevated troponins, an echocardiogram without RV dysfunction would stratify them into a lower-risk category (intermediate-low risk), thereby avoiding invasive procedures, and warrant only anticoagulation compared with patients with echocardiographic evidence of RV dysfunction (intermediate-high risk) who are at a higher risk of hemodynamic decompensation.[12] In patients that are hemodynamically unstable, an echocardiogram can be used to rule out other causes of shock such as pericardial tamponade, systolic left ventricular failure, acute severe valvular dysfunction, or aortic dissection.[12] In patients with suspected PE and high pretest probability who are too hemodynamically unstable to undergo a CT-PA, an echocardiogram can also be useful to identify certain findings of RV dysfunction that can warrant emergency reperfusion or pulmonary artery debulking therapies.[12]

Prognostic Use of Echocardiographic Findings in PE

Right Ventricular Dilatation, Dysfunction, and Failure. Hemodynamic decompensation in acute PE is caused by an increase in RV afterload from increased pulmonary vascular resistance (PVR) due to obstruction of the pulmonary arteries and vasoactive mediators.[15] Ultimately, this leads to decreased left ventricular filling and a reduction in cardiac output and hypotension.[16] If the right ventricle (RV) is unable to cope with the increased PVR and maintain antegrade flow, RV failure develops. This can be described as a clinical syndrome characterized by increased RV afterload and/or preload resulting in systemic congestion.[16] A failing RV is unable to mount high pulmonary pressures and often will have only modest elevations in pulmonary pressures.

In comparison, RV dysfunction that is out of proportion to the degree of overload can be identified by the presence of abnormal RV function parameters, segmental RV wall motion abnormality, and/or measures of RV–pulmonary artery coupling that are described later. Therefore, RV dysfunction requires the combination of Doppler and two-dimensional imaging. Right ventricular dysfunction has been seen in 31% of normotensive patients with PE, and these patients had an increased risk of hemodynamic decompensation and in-hospital mortality.[17] Consequently, it is crucial to identify these patients who will need escalation of therapies beyond anticoagulation. Multiple parameters of RV function are described below.

Right Ventricular Dilatation. The RV should appear less than two-thirds the size of the left ventricle (LV) on the standard apical 4-chamber view on echocardiography. As mentioned above, in the setting of increased RV afterload, pressure overload, and RV failure, RV dilatation occurs. On CT scan, a ratio of RV/LV dimension >0.9 predicted adverse events in patients with acute PE.[18,19]

On a TTE, RV measurements should be made from an RV-focused view on an apical 4-chamber view. A basal diameter of >41 mm or midlevel diameter of >35 mm indicates RV dilatation.[20] Aside

HIGHLIGHTS

- Intermediate- to high-risk PE patients pose a therapeutic challenge.
- Echocardiographic findings have prognostic value in the management of PE.
- Every parameter has its own set of limitations.

from the quantitative evaluation, RV dilatation can also be assessed qualitatively. Normally, the apex of the heart should be formed by the LV. In patients with RV dilatation, RV increases in size to form the apex. This qualitative evaluation can be used when the RV measures within normal limits despite it appearing to be larger than an LV that is underfilled.[21] Obtaining accurate RV dimensions by two-dimensional imaging are challenging and highly dependent on the operator as a focused RV view without foreshortening is necessary to get appropriate dimensions.

Parameters of RV Systolic Function. There are multiple echocardiographic parameters to assess RV systolic function. These include TAPSE, RV FAC, RV free wall strain, RV Tei index, and tissue Doppler-derived myocardial velocity (S').[22,23]

Tricuspid annular planar systolic excursion is determined from longitudinal displacement of the lateral tricuspid annulus between end diastole and systole on M mode.[20,21] It is reflective of the longitudinal RV function and not of the global RV function. However, it has been shown to have good correlation with RV ejection fraction (EF) measured on a radionuclide scan. It is easily obtainable and is less dependent on image quality, with good interobserver reliability. A systolic excursion of <1.7 cm is indicative of RV dysfunction. On occasion, it can give artifactually high or low values for RV function due to heart motion.[20]

Right ventricular Tei index or RV index of myocardial performance is a measure of global RV function. It is calculated by dividing the RV isovolumic time (isovolumic contraction plus isovolumic relaxation) by the ejection time, the upper limit of which is 0.43 when obtained by pulsed-wave (PW) Doppler and 0.54 when obtained by tissue Doppler imaging.[20] While measuring intervals for the RV Tei index using pulsed-wave Doppler, beats should have similar R-R intervals. The RV Tei index measurement by tissue Doppler imaging does not have this limitation because all the measurements are made on the same beat. However, the Tei index, regardless of method of measurement, can be falsely low in conditions with elevated right atrial pressures (RAPs).[20]

Right ventricular FAC is measured by the difference of the RV end-diastolic area and the end-systolic area divided by the RV end-diastolic area, after which it can be converted to a percentage. This is a measure of both radial and longitudinal RV function. An RV FAC <35% is indicative of RV systolic dysfunction. This is another measure that is highly dependent on the quality of the image as it should be measured on an RV-focused apical 4-chamber view, where the reader can visualize the free wall and the apex. The measurements can even vary among different readers.[20,21]

Right ventricular global longitudinal free wall strain is obtained by speckle-tracking and averaged over the 3 segments of the RV free wall in an RV-focused apical 4-chamber view. Right ventricular free wall strain more than −20% (<20% in absolute value) is abnormal.[20] Strain is the percentage change in free wall contraction from base to the apex. It requires additional imaging equipment and software for offline calculation. It is angle independent, with a certain amount of variation between different vendors, and can give a falsely low strain value if the basal reference points are placed on the atrial side of the tricuspid annulus.

Right ventricular lateral annular systolic velocity (S') is obtained by pulsed tissue Doppler and consists of the highest systolic velocity of RV excursion.[20] It is measured on the basal segment of the free wall side of the RV on an apical 4-chamber view. It is easily reproducible for the basal segment of the RV free wall, but it is not reproducible for mid and apical segments. It has similar limitations such as TAPSE. It was also shown to have good correlation when compared with EFs derived from radionuclide studies. A measurement of <10 cm/sec raises concern of abnormal RV systolic function.[21]

Some of the above (RV index of myocardial performance, FAC) are measures of global RV function, and others (TAPSE, S', free wall strain) are solely measures of longitudinal function of the RV. While longitudinal function contributes more to the RV stroke volume than the radial function, it has also been seen that relying only on measures of longitudinal function of the RV may be inadequate in evaluating the global function.[24,25] Due to regional variation of the RV in PE, parameters of longitudinal function can be falsely normal on occasion, and hence further assessment with a global function parameter would help characterize RV function accurately.

Some of these signs were evaluated as prognostic markers in PE. In one multivariate analysis, it was seen that TAPSE ≤1.5 cm was a better predictor of PE-related mortality than the CT RV/LV ratio and that TAPSE >2 cm could be used to identify a very low risk group.[26,27] However, this was not reflected in other studies. A few reports have found that TAPSE, FAC, S', and subjective RV size assessment were not associated with PE-related mortality.[22,28] In fact, RV free wall strain along with Tei index were the 2 factors that were independently associated with PE-related mortality.[22] Right ventricular global and segmental strain were noted to be reduced in higher-risk PE and associated with an increased 30-day and 60-day PE-related mortality.[29] Values obtained by tissue Doppler imaging were found to be associated with a lesser sensitivity for the diagnosis of PE.[23] Similarly, some of the other findings of RV dysfunction can be seen in other cardiopulmonary conditions in the absence of PE and therefore are not diagnostic.

The abnormal values in the above parameters have been summarized in Table 1. These values for RV dysfunction are not indexed to body surface area, gender, or ethnicity. The amount of data available was insufficient to classify RV dysfunction into mild, moderate, and severe.[21]

Measures of Stroke Volume. *Left Ventricular Outflow Tract VTI and RVOT VTI.* Left ventricular outflow tract VTI is an echocardiographic parameter that is commonly used to evaluate LVSV and cardiac output. Pulsed-wave Doppler of the LVOT to obtain the VTI and the cross-sectional area of the LVOT are commonly used to calculate the stroke volume.[30] In a retrospective analysis, Yuriditsky *et al.*[28] aimed to evaluate the association of a low LVOT VTI of ≤15 cm with hospital mortality, cardiac arrest, shock, or need for reperfusion in patients with PE. The study had 58% intermediate-risk patients and 6% patients with high-risk PE. They found that a low VTI had an odds ratio (OR) of 6 for the composite outcome of death or cardiac arrest and an OR of 23 for the composite outcome of shock or need for reperfusion. In comparison, TAPSE of <1.7 cm and tissue Doppler S' <10 cm/sec were not significantly associated with death or arrest in this study. The majority (85%) of patients in this study with a low VTI had RV dysfunction. Fifty-eight percent of intermediate- to high-risk PE patients had low VTI, and in comparison, only 5.8% of the low-risk patients had a low VTI. In this study, low VTI was the

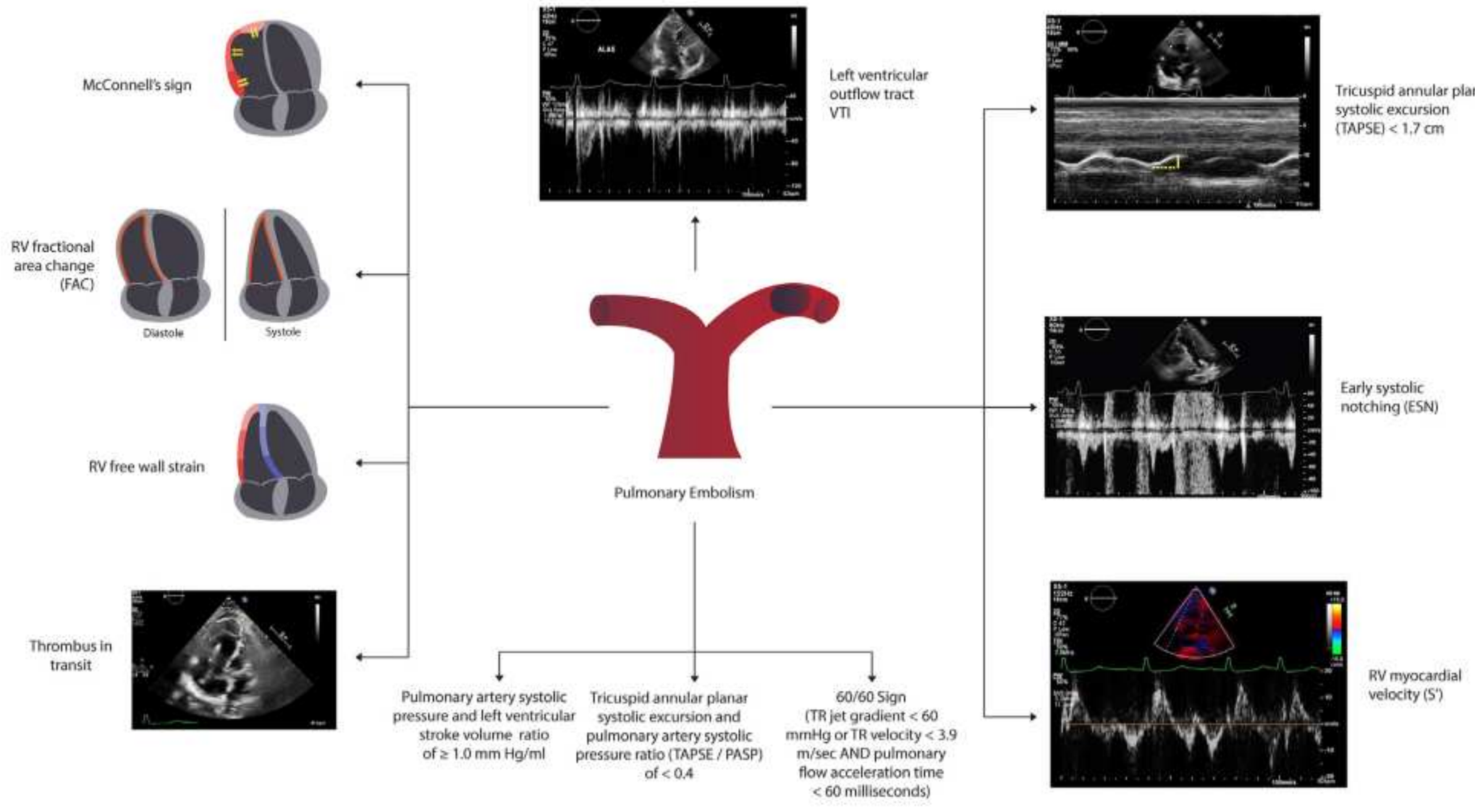
McConnell's sign
RV fractional area change (FAC)
Diastole
Systole
RV free wall strain
Thrombus in transit
Left ventricular outflow tract VTI
Pulmonary Embolism
Tricuspid annular plane systolic excursion (TAPSE) < 1.7 cm
Early systolic notching (ESN)
RV myocardial velocity (S')
Pulmonary artery systolic pressure and left ventricular stroke volume ratio of ≥ 1.0 mm Hg/ml
Tricuspid annular planar systolic excursion and pulmonary artery systolic pressure ratio (TAPSE / PASP) of < 0.4
60/60 Sign (TR jet gradient < 60 mmHg or TR velocity < 3.9 m/sec AND pulmonary flow acceleration time < 60 milliseconds)

Figure 1 A pictorial summary of different echocardiographic findings that can be used to risk stratify patients with PE. Right ventricular fractional area shortening, TAPSE, and S' are indicators of RV dysfunction. An LVOT VTI ≤ 15 cm and RVOT VTI < 9.5 cm have been shown to predict adverse outcomes. Abnormal PASP/LVSV, TAPSE/PASP, and ESN are also predictors of adverse outcomes in these patients. *TR*, Tricuspid regurgitation.

only factor that was significantly associated with mortality, cardiac arrest, shock, or need for reperfusion. Using reperfusion as a clinical endpoint represents one of the limitations of the study. The decision to reperfuse is a physician-dependent decision, and it is difficult to determine whether the patients that underwent reperfusion were truly the highest-risk patients. Another study of intermediate- to high-risk patients from the pulmonary embolism response team (PERT) activations revealed that patients who had hemodynamic deterioration or a cardiac arrest had a lower LVOT VTI compared with those who did not (12.9 cm vs 16.4 cm; $P = .011$).[31]

Subvalvular stenosis, dynamic LVOT obstruction, and significant aortic valve insufficiency are examples of clinical situations that can render LVOT VTI inaccurate for the assessment of forward stroke volume.

Table 1 Summary of abnormal values for RV size and parameters of RV function

Echo parameters	Abnormal RV function
RV size	Basal diameter > 41 mm
	Mid diameter > 35 mm
TAPSE	< 1.7 cm
RV fractional area shortening, %	< 35
RV Tei index	>0.43 (PW)
	> 0.54 (tissue Doppler)
Tissue Doppler myocardial velocity (S')	< 10 cm/sec
RV free wall strain	>−20% (<20% in absolute value)

Like the LVOT VTI, RVOT VTI using PW Doppler can be used to calculate RV stroke volume. In a study performed on 174 patients with intermediate-risk PE who underwent catheter-based intervention, the authors aimed to identify echocardiographic predictors of low cardiac index.[32] The findings of a low cardiac index were confirmed by right heart catheterization that showed 46% of this patient population had a low cardiac index. Even though LVOT VTI can be used to calculate cardiac output, the authors found that out of all the parameters, it was the RVOT VTI that best predicted a low cardiac index. An RVOT VTI of <9.5 cm was noted to be predictive of a low cardiac index and adverse outcomes. These were the patients that required escalation of care and underwent catheter-based interventions. Additionally, a low cardiac index was present despite normotension in these patients. In this study, intermediate-risk patients were defined by a systolic blood pressure >90 mm Hg and imaging (CT and/or TTE) *or* laboratory (elevated troponin and/or B-type natriuretic peptide) evidence of RV dysfunction. Right ventricular outflow tract VTI was also indicative of a low cardiac index and high rate of decompensation in intermediate-high risk PE patients in a different study.[31] The intermediate- to high-risk patients that decompensated had a lower RVOT VTI compared with those who did not (7.3 cm vs 10.7 cm; $P = .02$).

Reduced LVOT VTI identifies patients who have a reduced cardiac index, due to reduced filling from a failing RV, which is characterized by a reduced RVOT VTI. This is a result of being unable to cope with an acute increase in PVR and PASPs in the setting of an acute PE. Hence, these 2 noninvasive findings are useful as prognostic markers to point toward patients with subclinical shock that may warrant advanced therapies.

Compared with measuring LVOT VTI, RVOT VTI measurement poses a challenge. Inability to align the Doppler signal parallel to the

outflow tract without exceeding 20° will lead to underestimation of velocities. A reduced cardiac index based on calculations from a reduced RVOT VTI also assumes the absence of any outflow tract obstruction.

Measures of RV Function and Afterload. *Ratio of TAPSE and PASP (TAPSE/PASP).* Tricuspid annular planar systolic excursion measures the displacement of the lateral tricuspid annulus to the apex during RV contraction. Accordingly, the less the tricuspid annulus is displaced, the worse the RV EF, with a value of <1.7 cm considered abnormal.[21] Pulmonary artery systolic pressure is measured on echocardiogram by adding the maximum RV – right atrial gradient (derived by using the maximum tricuspid regurgitation velocity) to the central venous pressure (measured by diameter and respiratory collapse of the inferior vena cava [IVC]) in the absence of any significant pulmonary stenosis. If the IVC diameter is <2.1 cm and collapses >50% with respiration, it suggests a RAP of 3 mm Hg. If the IVC measures >2.1 cm and collapses <50% with respiration, the RAP is 15 mm Hg. In situations, where the IVC does not follow any of the above 2 patterns, the RAP is graded as 8 mm Hg.[21]

Pulmonary artery systolic pressure is a measure of the afterload the RV must overcome during systolic ejection. Both TAPSE and PASP have been known to be individual measures of RV function, but when evaluated together, they correlate with RV–pulmonary artery coupling. It has been shown to have prognostic value in pulmonary hypertension and systolic heart failure as well.[33] Typically, RV responds to an increase in afterload by increasing contractility. With increasing afterload and impaired RV contractile reserve, RV dilation and ultimately RV uncoupling occur. The ratio will decrease with a decrease in TAPSE or an increase in RV afterload, as measured by the PASP. A ratio of TAPSE/PASP <0.4 can predict the risk of hemodynamic deterioration and/or mortality in patients with acute PE.[33,34] A normal TAPSE/PASP ratio is 0.8 to 1.8. In certain situations, the ratio might not accurately represent the relationship between RV function and increasing afterload. As the relationship between RV adaptation to increasing afterload and RV function is nonlinear, this ratio might be overestimated in a situation wherein a failing RV might not be able to develop high PASPs.[35] On the contrary, in patients with chronic pulmonary hypertension, the ratio will be lower than what is found in acute PE.[33] This is because a slower increase in pulmonary pressures over a longer time period allows the RV a greater amount of time to adapt to the increasing afterload. In these situations, pulmonary artery pressures can increase to high levels resulting in a lower ratio. The previously described limitations of TAPSE also apply to this ratio. Despite the above-mentioned limitations, this indicator can be useful as a prognostic tool in the appropriate clinical setting to determine clinical deterioration and guide escalation to more advanced therapies.

Ratio of PASP and LVSV (PASP/LVSV). A measure of RV afterload was developed by Kamran *et al.*[36] for risk stratification in intermediate- to high-risk PE patients. They aimed to predict a higher-risk subgroup within all patients undergoing a PERT evaluation and requiring escalation of care. They compared the ratio of PASP to LVSV with traditional risk stratification scores. The primary outcome of this study was hospital mortality, cardiac arrest, and need for advanced therapies. They found that patients with a PASP/LVSV of ≥1.0 mm Hg/mL outperformed traditional PE risk stratification scores and were more likely to predict intermediate- or high-risk PE. Left ventricular stroke volume is calculated by multiplying the LVOT area with the LVOT VTI obtained from the pulsed Doppler across the LVOT. Measurement of PASP is described above.

The PASP/LVSV is a measure of pulmonary artery elastance, which correlates with RV afterload and has been shown to be associated with increased mortality in patients with PE and pulmonary hypertension secondary to left heart disease.[37,38] In hemodynamically significant acute PE, hypotension results from a reduced LVSV, due to reduced filling from a failing RV in the setting of increased pulmonary artery pressures. Therefore, with increasing pulmonary artery pressures and/or a reduced LVSV, this ratio will worsen, reflecting the performance of both the RV and the LV. When left ventricular EF was evaluated in patients with higher and lower ratios, the authors noted no difference, suggesting that left ventricular EF had no role in predicting worse outcomes in these patients.[36] It was also seen that this ratio predicted outcomes better than LVOT VTI and RVOT VTI in patients that have not yet deteriorated.[36] Limitations include the expertise needed in obtaining an LVOT VTI and interobserver measurement variability.

Thrombus in Transit. When PE does occur after DVT, the thrombus typically courses through the venous system to vena cava, through the right atrium and RV to finally lodge in the pulmonary artery and its branches. In most cases of PE, most of the thrombus burden is deposited in the main pulmonary arterial system. However, there have been multiple case reports of visualized thrombus in transit seen during point-of-care ultrasound or echocardiography.[39-41] A thrombus in transit has a high mortality of 4% to 18%. Because of its propensity to cause immediate hemodynamic instability, these patients are classified as high risk and frequently require escalation of care, but the optimal management is debated. For patients with thrombus in transit, the mortality rate without therapy, anticoagulation, surgical embolectomy, and thrombolysis was reported at 100%, 28.6%, 23.8%, and 11.3%, respectively.[42] Another study that compared different modalities of treatment in patients with right heart thrombi and PE showed that both surgical embolectomy and thrombolysis performed significantly better than anticoagulation alone with an OR of 2.61 (95% CI, 0.90-7.58) and 4.83 (95% CI, 1.52-15.36), respectively.[43] The odds of survival were highest with thrombolysis (81.5%) compared with surgical embolectomy (71.5%), with no reported increase in complications. Thrombus in transit is usually seen only in a minority of patients but when seen isconfirmatory of an acute PE.[44] Therefore, the presence of a thrombus in transit has both diagnostic and prognostic purposes.

Diagnostic Use of Echocardiography in PE

Regional RV Wall Motion Abnormality. McConnell *et al.*[45] in 1996 described a characteristic RV regional wall motion pattern that was particular to acute PE patients with RV dysfunction. This pattern of RV mid free wall akinesia and normal motion of the RV apex was found in patients with PE and was called McConnell's sign. While the initial study reported a high specificity of 94%, it was later noted to not be a specific marker for the diagnosis of PE. Its sensitivity varies between 70% and 77%, and the positive predictive value varies between 57% and 71%.[45,46] It has also been reported in acute chest syndrome, RV myocardial infarction, and acute respiratory distress syndrome.[45,47,48] In summary, the presence of McConnell's sign in conjunction with other abnormal parameters of RV function may suggest an acute PE in the absence of other conditions; however, its absence does not rule it out.[44]

Measure of Increased RV Afterload. *The 60/60 Sign and Early Systolic Notching (ESN).* The 60/60 sign is defined as the presence of tricuspid regurgitation jet gradient of less than 60 mm Hg *and* pulmonary

flow acceleration time of less than 60 ms.[49] This parameter appears to be more objective and reproducible compared with McConnell's sign.[50] When the 60/60 sign was combined with McConnell's sign, these 2 signs had a sensitivity of 36% and specificity of 94% in diagnosing acute PE.[49] The presence of ESN seen on the PW Doppler of the RVOT has been reported in a high percentage (92%) of patients with acute intermediate-risk or high-risk PE, while it was only seen in 2% of patients with subsegmental PE.[51] Use of ESN in emergency room patients showed that it had a specificity of 97% and a lower sensitivity of 34% in identifying patients with a PE.[52] However, ESN can also be seen in several other conditions that can cause pulmonary hypertension, such as chronic obstructive pulmonary disease, obstructive sleep apnea, and valvular diseases in the absence of an acute PE.

The appearance of a short acceleration time and ESN was reflective of the degree of increased PVR and distance from the RVOT. The physiology underlying ESN is that, with increased PVR, RV forward flow is impeded by the retrograde pressure wave that arrives early in systole.[53] The presence of this sign could be an indicator of the inability of RV to cope with the increasing afterload and a marker of ventriculoarterial uncoupling.[53]

It is important to differentiate ESN from late systolic notching, which has been defined as notching in the terminal aspect of the Doppler signal without 2 distinct peaks. Even though patients with late systolic notching also have elevated pulmonary artery pressures, they have a lower PVR and higher pulmonary artery compliance when compared with patients with earlier notching.[54,55] While the presence of ESN can at least be used to risk stratify patients into the intermediate-risk category, the role of ESN as a prognostic marker is questionable. The presence of ESN to determine which patient with intermediate risk is going to deteriorate hemodynamically is debatable due to the potential limitations with respect to patient population, sampling site variability, and variation with heart rate.

In summary, while all of the above-mentioned parameters are important, every one of them might not be present in the same patient, depending on the severity of disease and the ability to obtain good-quality images. For example, in patients with segmental dysfunction of the RV with mid free wall motion abnormality, TAPSE and S′ might be within normal limits. However, a normal TAPSE and/or S′ will hold little clinical value in a patient with a decreased RVOT VTI, LVOT VTI, or elevated PASP/LVSV, which would suggest an increased risk of clinical deterioration.

Being a heterogenous group of patients, intermediate- to high-risk PE patients pose a therapeutic challenge to the PERTs. In the management of these patients, echocardiogram plays a crucial role in risk stratification and prognosis. It holds little value in the diagnosis of PE but can help support or confirm the diagnosis in patients with high pretest probability and absence of other comorbid conditions. The utilization of echocardiography in PE patients can help identify RV dysfunction, which plays a crucial role in determining the next therapeutic step and the prognosis of these patients. These parameters have not been compared against each other; hence, the superiority of one finding over the other cannot be established. However, the knowledge of the above is crucial, as the presence or absence of any of the above can aid in management.

CONCLUSION

The management of intermediate-risk PE remains a constantly evolving topic and often requires a multidisciplinary approach. Echocardiographic findings can help determine which subset of intermediate-risk PEs need therapies beyond anticoagulation. These parameters should be used in conjunction with the clinical picture and pretest probability of the patient to make the decision on the next best management intervention.

REFERENCES

1. Heit JA. The epidemiology of venous thromboembolism in the community. Arterioscler Thromb Vasc Biol 2008;28:370-2.
2. Goldhaber SZ, Bounameaux H. Pulmonary embolism and deep vein thrombosis. Lancet 2012;379:1835-46.
3. Turetz M, Sideris AT, Friedman OA, et al. Epidemiology, pathophysiology, and natural history of pulmonary embolism. Semin Intervent Radiol 2018;35:92-8.
4. Meignan M, Rosso J, Gauthier H, et al. Systematic lung scans reveal a high frequency of silent pulmonary embolism in patients with proximal deep venous thrombosis. Arch Intern Med 2000;160:159-64.
5. Alotaibi GS, Wu C, Senthilselvan A, et al. Secular trends in incidence and mortality of acute venous thromboembolism: the AB-VTE population-based study. Am J Med 2016;129:879.e19-25.
6. Horlander KT, Mannino DM, Leeper KV. Pulmonary embolism mortality in the United States, 1979-1998: an analysis using multiple-cause mortality data. Arch Intern Med 2003;163:1711-7.
7. Heit JA, Silverstein MD, Mohr DN, et al. Predictors of survival after deep vein thrombosis and pulmonary embolism: a population-based, cohort study. Arch Intern Med 1999;159:445-53.
8. Dabbouseh NM, Patel JJ, Bergl PA. Role of echocardiography in managing acute pulmonary embolism. Heart 2019;105:1785-92.
9. Wolf SJ, McCubbin TR, Feldhaus KM, et al. Prospective validation of wells criteria in the evaluation of patients with suspected pulmonary embolism. Ann Emerg Med 2004;44:503-10.
10. Kline JA, Courtney DM, Kabrhel C, et al. Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. J Thromb Haemost 2008;6:772-80.
11. Wicki J, Perneger TV, Junod AF, et al. Assessing clinical probability of pulmonary embolism in the emergency ward: a simple score. Arch Intern Med 2001;161:92-7.
12. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): the Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Heart J 2020;41:543-603.
13. Jaff MR, McMurtry MS, Archer SL, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension. Circulation 2011;123:1788-830.
14. Miniati M, Monti S, Pratali L, et al. Value of transthoracic echocardiography in the diagnosis of pulmonary embolism: results of a prospective study in unselected patients. Am J Med 2001;110:528-35.
15. Smulders YM. Pathophysiology and treatment of haemodynamic instability in acute pulmonary embolism: the pivotal role of pulmonary vasoconstriction. Cardiovasc Res 2000;48:23-33.
16. Harjola VP, Mebazaa A, Čelutkienė J, et al. Contemporary management of acute right ventricular failure: a statement from the heart failure association and the working group on pulmonary circulation and right ventricular function of the European society of Cardiology. Eur J Heart Fail 2016;18:226-41.
17. Grifoni S, Olivotto I, Cecchini P, et al. Short-term clinical outcome of patients with acute pulmonary embolism, normal blood pressure, and echocardiographic right ventricular dysfunction. Circulation 2000;101:2817-22.
18. Meinel FG, Nance JW, Schoepf UJ, et al. Predictive value of computed tomography in acute pulmonary embolism: systematic review and meta-analysis. Am J Med 2015;128:747-59.e2.

19. Quiroz R, Kucher N, Schoepf UJ, et al. Right ventricular enlargement on chest computed tomography: prognostic role in acute pulmonary embolism. Circulation 2004;109:2401-4.
20. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American society of echocardiography and the European association of cardiovascular imaging. J Am Soc Echocardiogr 2015;28:1-39.e14.
21. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American society of echocardiography. J Am Soc Echocardiogr 2010;23:685-713.
22. Dahhan T, Siddiqui I, Tapson VF, et al. Clinical and echocardiographic predictors of mortality in acute pulmonary embolism. Cardiovasc Ultrasound 2016;14:44.
23. Rodrigues ACT, Cordovil A, Monaco C, et al. Right ventricular assessment by tissue-Doppler echocardiography in acute pulmonary embolism. Arq Bras Cardiol 2013;100:524-30.
24. Carlsson M, Ugander M, Heiberg E, et al. The quantitative relationship between longitudinal and radial function in left, right, and total heart pumping in humans. Am J Physiol Heart Circ Physiol 2007;293:H636-44.
25. Lakatos BK, Nabeshima Y, Tokodi M, et al. Importance of nonlongitudinal motion components in right ventricular function: three-dimensional echocardiographic study in healthy volunteers. J Am Soc Echocardiogr 2020;33:995-1005.e1.
26. Pruszczyk P, Goliszek S, Lichodziejewska B, et al. Prognostic value of echocardiography in normotensive patients with acute pulmonary embolism. JACC Cardiovasc Imaging 2014;7:553-60.
27. Lobo JL, Holley A, Tapson V, et al. Prognostic significance of tricuspid annular displacement in normotensive patients with acute symptomatic pulmonary embolism. J Thromb Haemost 2014;12:1020-7.
28. Yuriditsky E, Mitchell OJ, Sibley RA, et al. Low left ventricular outflow tract velocity time integral is associated with poor outcomes in acute pulmonary embolism. Vasc Med 2020;25:133-40.
29. Alerhand S, Sundaram T, Gottlieb M. What are the echocardiographic findings of acute right ventricular strain that suggest pulmonary embolism? Anaesth Crit Care Pain Med 2021;40:100852.
30. Porter TR, Shillcutt SK, Adams MS, et al. Guidelines for the use of echocardiography as a monitor for therapeutic intervention in adults: a report from the American Society of Echocardiography. J Am Soc Echocardiogr 2015;28:40-56.
31. Yuriditsky E, Mitchell OJL, Sista AK, et al. Right ventricular stroke distance predicts death and clinical deterioration in patients with pulmonary embolism. Thromb Res 2020;195:29-34.
32. Brailovsky Y, Lakhter V, Weinberg I, et al. Right ventricular outflow Doppler predicts low cardiac index in intermediate risk pulmonary embolism. Clin Appl Thromb Hemost 2019;25:1076029619886062.
33. Lyhne MD, Kabrhel C, Giordano N, et al. The echocardiographic ratio tricuspid annular plane systolic excursion/pulmonary arterial systolic pressure predicts short-term adverse outcomes in acute pulmonary embolism. Eur Heart J Cardiovasc Imaging 2021;22:285-94.
34. Khosla A, Gomez JL, Singh I. Impaired right ventricular - pulmonary arterial uncoupling thresholds in acute pulmonary embolism. In: *D106. Noe Valley: Clots, COVID, and Lung Vascular Diseases*. New York, NY: American Thoracic Society International Conference Abstracts, American Thoracic Society, A5422; 2022.
35. French S, Amsallem M, Ouazani N, et al. Non-invasive right ventricular load adaptability indices in patients with scleroderma-associated pulmonary arterial hypertension. Pulm Circ 2018;8:2045894018788268.
36. Kamran H, Hariri EH, Iskandar J, et al. Simultaneous pulmonary artery pressure and left ventricle stroke volume assessment predicts adverse events in patients with pulmonary embolism. J Am Heart Assoc 2021;10:e019849.
37. Tampakakis E, Shah SJ, Borlaug BA, et al. Pulmonary effective arterial elastance as a measure of right ventricular afterload and its prognostic value in pulmonary hypertension due to left heart disease. Circ Heart Fail 2018;11:e004436.
38. Brener MI, Burkhoff D, Sunagawa K. Effective arterial elastance in the pulmonary arterial circulation. Circ Heart Fail 2020;13:e006591.
39. Ng J, Pelletier MP. Thrombus in transit. N Engl J Med 2019;380:e8.
40. Puello F, Harewood J, Lee C, et al. Thrombus in transit: the emergence of a deadly diagnosis. Chest 2017;152:A1021.
41. Kashfi S, Nasser MF, Soleiman A, et al. Clot in transit in a patient with protein S deficiency. Eur J Case Rep Intern Med 2022;9:003355.
42. Rose PS, Punjabi NM, Pearse DB. Treatment of right heart thromboemboli. Chest 2002;121:806-14.
43. Athappan G, Sengodan P, Chacko P, et al. Comparative efficacy of different modalities for treatment of right heart thrombi in transit: a pooled analysis. Vasc Med 2015;20:131-8.
44. Kurnicka K, Lichodziejewska B, Goliszek S, et al. Echocardiographic pattern of acute pulmonary embolism: analysis of 511 consecutive patients. J Am Soc Echocardiogr 2016;29:907-13.
45. McConnell MV, Solomon SD, Rayan ME, et al. Regional right ventricular dysfunction detected by echocardiography in acute pulmonary embolism. Am J Cardiol 1996;78:469-73.
46. Vaid U, Singer E, Marhefka GD, et al. Poor positive predictive value of McConnell's sign on transthoracic echocardiography for the diagnosis of acute pulmonary embolism. Hosp Pract (1995) 2013;41:23-7.
47. Shah P, Schleifer JW, Mookadam F, et al. Right ventricular myocardial infarction: an underrecognized aetiology of McConnell's sign. Eur Heart J Cardiovasc Imaging 2015;16:225.
48. McCutcheon JB, Schaffer P, Lyon M, et al. The McConnell sign is seen in patients with acute chest syndrome. J Ultrasound Med 2018;37:2433-7.
49. Kurzyna M, Torbicki A, Pruszczyk P, et al. Disturbed right ventricular ejection pattern as a new Doppler echocardiographic sign of acute pulmonary embolism. Am J Cardiol 2002;90:507-11.
50. Shah BR, Velamakanni SM, Patel A, et al. Analysis of the 60/60 sign and other right ventricular parameters by 2D transthoracic echocardiography as adjuncts to diagnosis of acute pulmonary embolism. Cureus 2021;13:e13800.
51. Afonso L, Sood A, Akintoye E, et al. A Doppler echocardiographic pulmonary flow marker of massive or submassive acute pulmonary embolus. J Am Soc Echocardiogr 2019;32:799-806.
52. Aslaner MA, Karbek Akarca F, Aksu ŞH, et al. Diagnostic accuracy of early systolic notching in pulmonary embolism. J Ultrasound Med 2022;41:637-44.
53. Bernard S, Namasivayam M, Dudzinski DM. Reflections on echocardiography in pulmonary embolism—Literally and Figuratively. J Am Soc Echocardiogr 2019;32:807-10.
54. Kushwaha SP, Zhao Q, Liu Q, et al. Shape of the pulmonary artery Doppler-flow profile predicts the hemodynamics of pulmonary hypertension caused by left-sided heart disease. Clin Cardiol 2016;39:150-6.
55. Arkles JS, Opotowsky AR, Ojeda J, et al. Shape of the right ventricular Doppler envelope predicts hemodynamics and right heart function in pulmonary hypertension. Am J Respir Crit Care Med 2011;183:268-76.